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Retrograde Menstruation in Healthy Women and in Patients With Endometriosis

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Blood was found in the peritoneal fluid in 90% of women with patent tubes at laparoscopy during perimenstrual time. If the fallopian tubes were occluded, then only 15% of patients had evidence of blood in the pelvis. Also, 90% of patients with endometriosis and eight of nine women on oral contraceptives had bloody fluid during the menstrual period. The present observations indicate that retrograde menstruation through the fallopian tubes into the peritoneal cavity is a very common physiologic event in all menstruating women with patent tubes. (*Obstet Gynecol* 64:151, 1984)

In 1927 Sampson proposed that endometriosis was due to implantation of endometrial cells during retrograde menstruation.¹ During his lifetime, most of the opponents of this theory dismissed it mainly on the basis that retrograde menstruation, although occasionally noted to occur, was a relatively rare phenomenon.^{2,3} Therefore, it would not explain the development of a common clinical entity such as endometriosis. Since that time, the frequency of retrograde menstruation has been debated.

No systematic studies documenting the incidence of retrograde menstruation have been published in spite of the fact that millions of women have undergone laparotomy or laparoscopy, making possible direct observations of pelvic structures. Recently, however, Blumenkrantz et al⁴ reported that nine of 11 menstruating women undergoing peritoneal dialysis had blood present regularly in the dialysate during the time of their period and in this way documented retrograde menstruation. They also suggested that this event was a rather common phenomenon, and not limited to women with renal failure. In addition, a study from the authors' institution reported that of 80 peritoneal fluid samples, all four obtained during menses were bloody.⁵

Based on laparoscopy of 323 women, the current study presents further evidence suggesting that retrograde menstruation occurs in most menstruating women who have open fallopian tubes.

Material and Methods

Between July 1980 and September 1983, 331 pelvic fluid samples were obtained from patients undergoing laparoscopy at The North Carolina Memorial Hospital. Of

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181 patients with patent tubes and normal pelves, 78 underwent laparoscopy for bilateral tubal ligation, and 103 were undergoing diagnostic laparoscopy for evaluation of infertility or chronic pelvic pain. Of 40 patients with occluded fallopian tubes, 16 had distal blockage, two had proximal blockage, and 22 had proximal occlusion as a result of previous tubal ligation. Eighty-one patients were noted to have mild to moderate endometriosis.

Peritoneal fluid was aspirated with an 18-gauge Silastic catheter through the operative channel of the laparoscope and collected into a heparin-containing test tube. The color of the fluid, when in the tube, was recorded either as straw, pink, or bloody. Upon reviewing the records of these patients, the date of the last normal menses in 302 patients, and observations on the fluid samples were available. In addition, 21 women who were on oral contraceptives were identified.

Because only visual documentation of the color of the fluid was available for all samples, an experiment was set up to test the accuracy of this technique in assessment of the presence of blood. A series of 30 tubes containing ten different concentrations of red blood cells (ranging from hematocrit of 0 to 10) in peritoneal fluid was constructed. The tubes were shown in a random order to each of the nine persons involved in classifying these fluids into one of the three color categories. The color was judged as straw when hematocrit was less than $0.5 \pm 0.2\%$ (SD) and bloody when hematocrit was higher than $3.2 \pm 2.0\%$. Between these values, the color was judged to be pink. The level of agreement between different individuals and by each individual between two testing occasions (the coefficient κ) was determined according to Cohen⁶

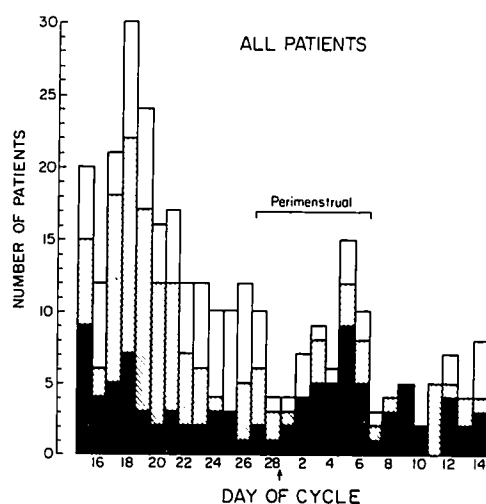


Figure 1. Appearance of all 302 peritoneal fluid samples obtained during laparoscopy. Solid bars = bloody; shaded bars = pink; open bars = straw.

Table 1. Appearance of Peritoneal Fluid Samples Obtained on Nonmenstrual Days 7 to 26

| | No endometriosis | | Endometriosis |
|----------------|------------------|--------------|---------------|
| | Open tubes | Closed tubes | |
| Straw | 54 | 11 | 14 |
| Pink or bloody | 85 | 16 | 57 |
| Total | 139 | 27 | 71 |

and Fleiss.⁷ Values of κ ranged from 0.39 to 1.0 between pairs of individuals and from 0.52 to 1.0 between the two testings.

Observations by Blumenkrantz et al⁴ suggested that the presence of blood in the peritoneal dialysates usually preceded the beginning of menstrual flow by one to two days. Therefore, the patients in this series were divided in two groups: 1) perimenstrual, if they underwent laparoscopy on days one to six or 27 to 30 of their cycle, and 2) nonmenstrual, if laparoscopy was performed between days 7 to 26 of the cycle.

Statistical analysis of the data was performed by using the χ^2 statistic for 2×2 contingency tables constructed for pairs of variables and normal approximation for the binomial distribution.⁸

Results

Figure 1 presents the noted color of each of the 302 fluid samples in perimenstrual and nonmenstrual phases of the cycle. It is obvious from the graph that there is an increased amount of blood in the pelvic cavity around the time of menses and also immediately after ovulation with clearance of that blood over the next five to six days.

As indicated in Table 1, a total of 237 fluid samples were obtained in the nonmenstrual phase. Overall one-third of these fluids were straw, and the other two-thirds contained an appreciable amount of red blood cells (either pink or bloody). In normal women with open fallopian tubes, 61.1% of fluids were either pink or bloody as compared with 60% in women with occluded tubes, suggesting that tubal patency is not an important factor for the presence of blood in the peritoneal cavity during the nonmenstrual phase of the

Table 2. Appearance of Peritoneal Fluid Samples Obtained on Perimenstrual Days 1 to 6 and 27 to 30

| | No endometriosis | | Endometriosis |
|----------------|------------------|--------------|---------------|
| | Open tubes | Closed tubes | |
| Straw | 4 | 11 | 1 |
| Pink or bloody | 38 | 2 | 9 |
| Total | 42 | 13 | 10 |

normal cycle. In the 12 women on oral contraceptives who underwent laparoscopy during this phase of the cycle, six had pink fluid in the cul-de-sac. In patients with endometriosis, blood was detected significantly more often ($P \leq .005$) than in other women with patent tubes in the nonmenstrual phase.

Table 2 presents corresponding data for fluid samples obtained during the perimenstrual phase of the cycle. Of 52 samples from women with patent fallopian tubes, 47 (90.4%) had an appreciable amount of red blood cells; 70% of these were grossly bloody. This is significantly different ($P \leq .001$) than the corresponding percentage in nonmenstrual samples. In the nine women on oral contraceptives who underwent laparoscopy in the perimenstrual phase, eight had bloody fluid. Only two of 13 (15.4%) patients with occluded tubes had red blood cells (one pink and one bloody sample) in the peritoneal fluid. This frequency is significantly lower ($P \leq .005$) than in women with open tubes. These figures clearly indicate that during the perimenstrual phase, the peritoneal fluid in almost all women, including those taking oral contraceptives, contains blood and that the fallopian tubes play an important role as conduits for menstrual blood.

Discussion

The important clinical observations by Blumenkrantz et al⁴ in women undergoing peritoneal dialysis indicated that bleeding into the dialysate usually was detectable one to two days before the menstrual period and during the menses. The recognition of this phenomenon prompted the authors to include the patients undergoing laparoscopy on these premenstrual days in the perimenstrual group rather than in the nonmenstrual group. The results of this study clearly indicate that during this perimenstrual time of the cycle, over 90% of normal and infertile women have blood in their peritoneal fluid. If the tubes are occluded, there is no correlation between the perimenstrual phase and the presence of blood in the pelvis. This indicates that the fallopian tubes are the major conduit for blood entering the peritoneal compartment at the time of menses.

The use of oral contraceptives has been advocated as a possible means of protection from endometriosis,^{5,9} but it may be inferred from the present data that if used noncontinuously, allowing menstruation to occur, retrograde menstruation will also occur, as these women consistently had blood in the pelvic fluid at this time. To prevent this, an uninterrupted mode of administration may be necessary.

Many studies have demonstrated that various volumes of peritoneal fluid are found in the female pelvis during laparoscopy.^{5,10,11} This fluid in the pelvis often

seems to contain blood.^{12,13} In 69% of all patients in this series, an appreciable amount of blood was detected. Sources of this blood include the abdominal wall stab wound(s) and severed vessels in omentum or adhesions in the pelvis. This contamination with fresh blood is always variably present in addition to blood derived from natural, physiologic phenomena like ovulation, and eventually, retrograde menstruation. It is not possible to accurately assess the impact of this contamination, but it may be safe to assume that this iatrogenic hemorrhage occurs at random and is not dependent on any particular time of the cycle. Furthermore, observation (not shown) that even grossly bloody peritoneal fluid samples obtained during menses did not contain appreciable numbers of granulocytes suggests that the blood did not result from an immediate hemorrhage to the pelvic compartment.

Sampson¹ originally suggested that retrograde menstruation provides a mechanism by which endometrial cells can implant on peritoneal surfaces in women with endometriosis. Because the great majority of the authors' patients either with or without endometriosis showed evidence of retrograde menstruation, it cannot explain why only some women have developed the disease. Other factors, either hormonal or immunologic, will apparently determine whether or not ectopic implantation can take place. Koninckx et al^{14,15} demonstrated a high incidence of luteinized unruptured follicle syndrome in women with endometriosis, and also a low, late luteal phase progesterone/estrogen ratio of peritoneal fluid in this syndrome. They hypothesized that this local hormonal imbalance may be critical in allowing endometrial cells, if present in the peritoneal compartment, to implant on the peritoneum. The results of the present study provide direct evidence that cells originating from the uterine cavity indeed are present in the pelvis in the late luteal phase preceding menses, and this theory may hold if peritoneal fluid hormone levels are abnormal. However, a recent study¹⁶ found no difference in progesterone and estrogen levels during this time in the fluid of women with or without endometriosis. However, several sources^{17,18} suggest that abnormal immunologic defense mechanisms may be operative in women with endometriosis, and this can explain the occurrence of ectopic implantation of endometrium. More detailed comparative information on both hormonal and immunologic function in a sizeable population of both normal women and patients with endometriosis is clearly warranted.

Studies on peritoneal macrophages^{5,19} have demonstrated that samples taken at menstruation usually have the highest concentrations of these cells, the majority of which are recent arrivals. It was suggested that this influx of phagocytic macrophages to the pelvis

is a response to retrograde menstruation. The present results clearly support this idea, and it remains to be seen whether or not the nucleated cellular components of menstrual detritus are also regularly transported through the fallopian tubes. Studies are in progress in The North Carolina Memorial Hospital to detect the presence of either epithelial or stromal cells of endometrial origin in peritoneal fluid.

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